

SEQUENCE LISTING

<110> WUCHERPFENNIG, Kai W STROMINGER, Jack L

<120> MONOVALENT, MULTIVALENT AND MULTIMERIC MHC BINDING DOMAIN FUSION PROTEINS AND CONJUGATES, AND USES THEREFOR

<130> HAR-005

<140> 09/248,964

<141> 1999-02-12

<150> PCT/US97/14503

<151> 1997-08-15

<150> 60/075,351

<151> 1998-02-19

<150> 60/024,007

<151> 1996-08-15

<160> 14

<170> PatentIn Ver. 2.0

<210> 1

<211> 750

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: DR2-Fos fusion

<220>

<221> CDS

<222> (1)..(735)

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<221> misc_feature

<222> (1)..(21)

<223> 3' end of secretory signal

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<221> misc_structure

<222> (22)..(594)

<223> DRA*0101 extracellular domain

<220>

<221> misc_feature

<222> (595)..(615)

<223> Linker sequence

<220>

<221> misc feature

<222> (616) .. (735) .



<223> Fos leucine zipper domain

							4	RADE	MA			
gta	0> 1 tct Ser										48	
	gag Glu										96	
	gat Asp										144	
	tgg Trp 50										192	
	gca Ala										240	
	aag Lys										288	RECEIVED
	gtg Val										336	JUL 31 2000
	tgt Cys										384	TECH CENTER 1600/2900
	cga Arg 130										432	RECEIVED
_	ccc Pro	 _	-			_					480	JUL 28200 3
	ccc Pro										528	TECH CENTER 1600/2900
	gat Asp										576	
	cca Pro										624	
	ctc Leu										672	

cag acc gag att gcc aat cta ctg aaa gag aag gaa aaa ctg gag ttc 720 Gln Thr Glu Ile Ala Asn Leu Leu Lys Glu Lys Glu Lys Leu Glu Phe 225 230 235 240

atc ctg gcc gcc cat tgagaattct atgac Ile Leu Ala Ala His 245 750

<210> 2 <211> 245 <212> PRT <213> Artificial Sequence

-100 > 2

Val Ser Leu Glu Lys Arg Glu Ile Lys Glu Glu His Val Ile Ile Gln
1 5 10 15

Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met Phe Asp 20 25 30

Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys Glu Thr 35 40 45

Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu Ala Gln 50 55 60

Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu Ile Met 65 70 75 80

Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro Glu Val 85 90 95

Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn Val Leu 100 105 110

Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val Thr Trp 115 120 125

Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val Ser Glu Thr Val Phe 130 135 140

Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu Pro Phe 145 150 155 160

Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His Trp Gly
165 170 175

Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe Asp Ala Pro Ser Pro 180 185 190

Leu Pro Glu Thr Thr Glu Val Asp Gly Gly Gly Gly Leu Thr Asp
195 200 205

Thr Leu Gln Ala Glu Thr Asp Gln Leu Glu Asp Glu Lys Ser Ala Leu

Gln Thr Glu Ile Ala Asn Leu Leu Lys Glu Lys Glu Lys Leu Glu Phe 230 Ile Leu Ala Ala His <210> 3 <211> 771 <212> DNA <213> Artificial Sequence <223> Description of Artificial Sequence: DR@-Jun fusion <221> CDS <222> (1)..(756) <220> <221> misc_feature <222> (1)..(21) <223> 3' end of sectetory signal <220> <221> misc_feature <222> (22)..(615) <223> DRB1*1501 extracellular domain <220> <221> misc feature <222> (616)..(636) <223> Linker sequence <220> <221> misc feature <222> (637)..(756) <223> Jun leucine zipper domain <400> 3 gta tct ctc gag aaa aga gag ggg gac acc cga cca cgt ttc ctg tgg Val Ser Leu Glu Lys Arg Glu Gly Asp Thr Arg Pro Arg Phe Leu Trp 1 cag cct aag agg gag tgt cat ttc ttc aat ggg acg gag cgg gtg cgg 96 Gln Pro Lys Arg Glu Cys His Phe Phe Asn Gly Thr Glu Arg Val Arg 20 ttc ctg gac aga tac ttc tat aac cag gag gag tcc gtg cgc ttc gac 144 Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu Glu Ser Val Arg Phe Asp 35

age gac gtg ggg gag tte egg geg gtg aeg gag etg ggg egg eet gae

Ser Asp Val Gly Glu Phe Arg Ala Val Thr Glu Leu Gly Arg Pro Asp

192

`	EMARIE	,													
טַ	gct	gag			aac Asn										240
					tac Tyr 85										288
					cga Arg										336
					cag Gln										384
					agc Ser										432
					atg Met										480
					ctg Leu 165										528
					caa Gln										576
					gca Ala										624
			Gly	Gly	cgc Arg	Ile	Ala	Arg	Glu	Glu					672
					tcg Ser										720
					ctt Leu 245						tgag	gaatt	ct a	itgac	771

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<212> PRT

<213> Artificial Sequence

<400> 4

Val Ser Leu Glu Lys Arg Glu Gly Asp Thr Arg Pro Arg Phe Leu Trp

5 10 15

Gln Pro Lys Arg Glu Cys His Phe Phe Asn Gly Thr Glu Arg Val Arg 20 25 30

Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu Glu Ser Val Arg Phe Asp 35 40 45

Ser Asp Val Gly Glu Phe Arg Ala Val Thr Glu Leu Gly Arg Pro Asp 50 55 60

Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu Gln Ala Arg Ala 65 70 75 80

Ala Val Asp Thr Tyr Cys Arg His Asn Tyr Gly Val Val Glu Ser Phe
85 90 95

Thr Val Gln Arg Arg Val Gln Pro Lys Val Thr Val Tyr Pro Ser Lys
100 105 110

Thr Gln Pro Leu Gln His His Asn Leu Leu Val Cys Ser Val Ser Gly
115 120 . 125

Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp Phe Leu Asn Gly Gln Glu 130 135 140

Glu Lys Ala Gly Met Val Ser Thr Gly Leu Ile Gln Asn Gly Asp Trp 145 150 155 160

Thr Phe Gln Thr Leu Val Met Leu Glu Thr Val Pro Arg Ser Gly Glu 165 170 175

Val Tyr Thr Cys Gln Val Glu His Pro Ser Val Thr Ser Pro Leu Thr 180 185 190

Val Glu Trp Arg Ala Arg Ser Glu Ser Ala Gln Ser Lys Val Asp Gly
195 200 205

Gly Gly Gly Arg Ile Ala Arg Leu Glu Glu Lys Val Lys Thr Leu 210 215 220

Lys Ala Gln Asn Ser Glu Leu Ala Ser Thr Ala Asn Met Leu Arg Glu 225 230 235 240

Gln Val Ala Gln Leu Lys Gln Lys Val Met Asn His 245 250

<210> 5

<211> 42

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic PCR primer

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<223> Description of Artificial Sequence: Synthetic PCR
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gtcatagaat tctcaatggg cggccaggat gaactccag
                                                                    39
<210> 7
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<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic PCR
      primer
<400> 7
                                                                    42
gtatctctcg agaaaagaga gggggacacc cgaccacgtt tc
<210> 8
<211> 39
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Synthetic PCR
      primer
<400> 8
gtcatagaat tctcaatggt tcatgacttt ctgtttaag
                                                                    39
<210> 9
<211> 14
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic,
      biotin ligase recognition sequence
<400> 9
Leu Gly Gly Ile Phe Glu Ala Met Lys Met Glu Leu Arg Asp
                  5
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<210> 10
<211> 16
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Synthetic,
      linker sequence
<400> 10
Ser Gly Gly Gly Ser Leu Val Pro Arg Gly Ser Gly Gly Gly Ser
<210> 11
<211> 1446
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: DR2-IgG fusion
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<221> misc_feature
<222> (1)..(15)
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<222> (16)..(588)
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<222> (589)..(609)
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<221> misc_feature
<222> (610)..(729)
<223> Fos leucine zipper domain
<220>
<221> misc feature
<222> (730)..(1437)
<223> IgG domain
ctc gag aaa aga gag atc aaa gaa gaa cat gtg atc atc cag gcc gag
Leu Glu Lys Arg Glu Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu
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ttc tat ctg aat cct gac caa tca ggc gag ttt atg ttt gac ttt gat

48

96

Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp ggt gat gag att ttc cat gtg gat atg gca aag aag gag acg gtc tgg 144 Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys Glu Thr Val Trp 35 cqq ctt qaa qaa ttt qqa cqa ttt qcc aqc ttt qaq qct caa qqt qca 192 Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala ttg gcc aac ata gct gtg gac aaa gcc aac ttg gaa atc atg aca aag 240 Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys ege tee aac tat act eeg ate ace aat gta eet eea gag gta act gtg 288 Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val 90 ctc acg aac agc cct gtg gaa ctg aga gag ccc aac gtc ctc atc tgt 336 Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys 100 105 110 ttc ata gac aag ttc acc cca cca gtg gtc aat gtc acg tgg ctt cga 384 Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg 115 120 125 aat gga aaa cct gtc acc aca gga gtg tca gag aca gtc ttc ctg ccc 432 Asn Gly Lys Pro Val Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro 130 135 agg gaa gac cac ctt ttc cgc aag ttc cac tat ctc ccc ttc ctg ccc 480 Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro 145 150 tca act gag gac gtt tac gac tgc agg gtg gag cac tgg ggc ttg gat 528 Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp 170 gag cct ctt ctc aag cac tgg gag ttt gat gct cca agc cct ctc cca 576 Glu Pro Leu Lys His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro 180 185 gag act aca gag gtc gac gga ggt ggc ggt tta act gat aca ctc 624 Glu Thr Thr Glu Val Asp Gly Gly Gly Gly Leu Thr Asp Thr Leu 195 200 caa gcg gag aca gat caa ctt gaa gac gag aag tct gcg ttg cag acc 672 Gln Ala Glu Thr Asp Gln Leu Glu Asp Glu Lys Ser Ala Leu Gln Thr 210 215 gag att gcc aat cta ctg aaa gag aag gaa aaa ctg gag ttc atc ctg 720 Glu Ile Ala Asn Leu Leu Lys Glu Lys Glu Lys Leu Glu Phe Ile Leu 225 230 235

gcc gcc cat gca gca tct gag ccc aga ggg ccc aca atc aag ccc tgt Ala Ala His Ala Ala Ser Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys



245 250 255

					cca Pro										816
					aag Lys										864
					gtg Val										912
					ttt Phe 310										960
					gag Glu										1008
					cac His										1056
					aaa Lys							 _			1104
					tca Ser	-	-	_		_	_	_	_		1152
					atg Met 390										1200
					cct Pro										1248
					aac Asn										1296
					atg Met										1344
	gtg	_	_		agc			_			_			_	1392
_	Val 450	Glu	Arg	Asn	ser	455	Der	0,0	202	741	460	 	O ₁	Deu	



<210> 12

<211> 479

<212> PRT

<213> Artificial Sequence

<400> 12

Leu Glu Lys Arg Glu Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu
1 5 10 15

Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp 20 25 30

Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys Glu Thr Val Trp
35 40 45

Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala
50 55 60

Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys
65 70 75 80

Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val 85 90 95

Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys
100 105 110

Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg 115 120 125

Asn Gly Lys Pro Val Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro 130 135 140

Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro 145 150 155 /160

Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp 165 170 175

Glu Pro Leu Lys His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro 180 185 190

Glu Thr Thr Glu Val Asp Gly Gly Gly Gly Leu Thr Asp Thr Leu
195 200 205

Gln Ala Glu Thr Asp Gln Leu Glu Asp Glu Lys Ser Ala Leu Gln Thr 210 215 220

Glu Ile Ala Asn Leu Leu Lys Glu Lys Glu Lys Leu Glu Phe Ile Leu 225 230 235 240

Ala Ala His Ala Ala Ser Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys 245 250 255 JUL 2 1 2000 JUL 2

Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Gly Pro Ser Val 260 265 270

Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser 275 280 285

Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp 290 295 300

Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala Gln 305 310 315 320

Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser 325 330 335

Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe Lys 340 345 350

Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile 355 360 365

Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu Pro 370 375 380

Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys Met 385 390 395 400

Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn 405 410 415

Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser 420 425 430

Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn 435 440 445

Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly Leu 450 455 460

His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys 465 470 475

<210> 13

<211> 1851

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: DR2-IgM fusion

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<221> CDS

<222> (1)..(1836)

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<222> (649)..(669)
<223> Linker
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<221> misc feature
<222> (670)..(789)
<223> Fos leucine zipper domain
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<222> (790)..(1836)
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Met Ala Ile Ser Gly Val Pro Val Leu Gly Phe Phe Ile Ile Ala Val
ctg atg agc gct cag gaa tca tgg gct atc aaa gaa gaa cat gtg atc
                                                                   96
Leu Met Ser Ala Gln Glu Ser Trp Ala Ile Lys Glu Glu His Val Ile
atc cag gcc gag ttc tat ctg aat cct gac caa tca ggc gag ttt atg
                                                                   144
Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met
         35
ttt gac ttt gat ggt gat gag att ttc cat gtg gat atg gca aag aag
                                                                   192
Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys
     50
gag acg gtc tgg cgg ctt gaa gaa ttt gga cga ttt gcc agc ttt gag
                                                                   240
Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu
gct caa ggt gca ttg gcc aac ata gct gtg gac aaa gcc aac ttg gaa
                                                                   288
Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu
atc atg aca aag cgc tcc aac tat act ccg atc acc aat gta cct cca
                                                                   336
Ile Met Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro
            100
gag gta act gtg ctc acg aac agc cct gtg gaa ctg aga gag ccc aac
                                                                   384
Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn
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125

115

011	£ /														
JUL 2 1 2				•											
PARADEN	Val	ctc			ttc Phe										432
					aat Asn										480
					agg Arg 165										528
·					tca Ser										576
-			_	_	gag Glu			_				_	_		624
÷					gag Glu										672
		_			caa Gln			_		_	_		_		720
	_		_		gag Glu 245									-	768
					gcc Ala										816
					cca Pro										864
					tgc Cys										912
					aag Lys										960
-	_	_			atc Ile 325	_								_	1008
					ctt Leu										1056

gtg tac acc tgc cgt gtg gat cac agg ggt ctc acc ttc ttg aag aac 1104

Val	Tyr	Thr 355	Cys	Arg	Val	Asp	His 360	Arg	Gly	Leu	Thr	Phe 365	Leu	Lys	Asn		PATER
				_	_	_	_				gat Asp 380					1152	
						_	_				agc Ser	_		_		1200	

tcc	tgg	gct	tct	caa	agt	ggt	gaa	cca	ctg	gaa	acc	aaa	att	aaa	atc	1296
Ser	Trp	Ala	Ser	Gln	Ser	Gly	Glu	Pro	Leu	Glu	Thr	Lys	Ile	Lys	Ile	
			420					425					430			

ctg acc tgt ctg gtc tca aac ctg gca acc tat gaa acc ctg agt atc Leu Thr Cys Leu Val Ser Asn Leu Ala Thr Tyr Glu Thr Leu Ser Ile

atg Met	_					_	_	_		-	_	_	1344
		435			440				445				

gtt Val	_	 _	_	~~		~ ~	_	~		 _		1392
	450				455				460			

act	cac	agg	gat	ctg	cct	tca	cca	cag	aag	aaa	ttc	atc	tca	aaa	ccc	1440
Thr	His	Arg	Asp	Leu	Pro	Ser	Pro	Gln	Lys	Lys	Phe	Ile	Ser	Lys	Pro	
465					470					475					480	

			~~~													1400
aat	gag	gcg	cac	aaa	cat	cca	CCL	get	grg	Lac	etg	ctg	cca	cca	get	1488
Asn	Glu	Val	His	Lys	His	Pro	Pro	Ala	Val	Tyr	Leu	Leu	Pro	Pro	Ala	
				485					490	_				495		

cgt	gaa	caa	ctg	aac	ctg	agg	gag	tca	gcc	aca	gtc	acc	tgc	ctg	gtg	1536
Arg	Glu	Gln	Leu	Asn	Leu	Arg	Glu	Ser	Ala	Thr	Val	Thr	Cys	Leu	Val	
			500					505					510			

ааст	aac	ttc	tet	act	σca	gac	atc	tct	ata	caa	t.aa	aaσ	cag	agg	ggc	1584
Lys					_	_						_	_			
•	•	515				_	520				-	525			-	

cag	ctc	tta	CCC	cag	gag	aag	tat	gtg	acc	agt	gcc	ccg	atg	cca	gag	1632
Gln	Leu	Leu	Pro	Gln	Glu	Lys	Tyr	Val	Thr	Ser	Ala	Pro	Met	Pro	Glu	
	530					535					540					

cct	qqq	qcc	cca	ggc	ttc	tac	ttt	acc	cac	agc	atc	ctg	act	gtg	aca	1680
Pro	Gly	Āla	Pro	Gly	Phe	Tyr	Phe	Thr	His	Ser	Ile	Leu	Thr	Val	Thr	
545	-			_	550	,				555					560	

* - * · · · · · · · · · · · · · · · · ·			gag acc tat acc tg Glu Thr Tyr Thr Cys 570	
-----------------------------------------	--	--	--------------------------------------------------	--

gag	gcc	ctg	cca	cac	ctg	gtg	acc	gag	agg	acc	gtg	gac	aag	tcc	act	1776
Glu	Ala	Leu	Pro	His	Leu	Val	Thr	Glu	Arg	Thr	Val	Asp	Lys	Ser	Thr	

ggt aaa ccc aca ctg tac aat gtc tcc ctg atc atg tct gac aca ggc 1824 Gly Lys Pro Thr Leu Tyr Asn Val Ser Leu Ile Met Ser Asp Thr Gly

95 600 60

ggc acc tgc tat tgaagatetg tegac Gly Thr Cys Tyr 610 1851

590

<210> 14

<211> 612

<212> PRT

<213> Artificial Sequence

<400> 14

Met Ala Ile Ser Gly Val Pro Val Leu Gly Phe Phe Ile Ile Ala Val 1 5 10 15

Leu Met Ser Ala Gln Glu Ser Trp Ala Ile Lys Glu Glu His Val Ile 20 25 30

Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met
35 40 45

Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys
50 55 60

Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu 65 70 75 80

Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu 85 90 95

Ile Met Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro
100 105 110

Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn 115 120 125

Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val 130 135 140

Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val Ser Glu Thr 145 150 155 160

Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu 165 170 175

Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His
180 185 190

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe Asp Ala Pro 195 200 205

Ser Pro Leu Pro Glu Thr Thr Glu Val Asp Gly Gly Gly Gly Leu

210 215 220

Thr 225	Asp	Thr	Leu	Gln	Ala 230	Glu	Thr	Asp	Gln	Leu 235	Glu	Asp	Glu	Lys	Ser 240
Ala	Leu	Gln	Thr	Glu 245	Ile	Ala	Asn	Leu	Leu 250	Lys	Glu	Lys	Glu	Lys 255	Leu
Glu	Phe	Ile	Leu 260	Ala	Ala	His	Val	Ala 265	Glu	Met	Asn	Pro	Asn 270	Val	Asn
Val	Phe	Val 275	Pro	Pro	Arg	Asp	Gly 280	Phe	Ser	Gly	Pro	Ala 285	Pro	Arg	Lys
Ser	Lys 290	Leu	Ile	Cys	Glu	Ala 295	Thr	Asn	Phe	Thr	Pro 300	Lys	Pro	Ile	Thr
Val 305	Ser	Trp	Leu	Lys	Asp 310	Gly	Lys	Leu	Val	Glu 315	Ser	Gly	Phe	Thr	Thr 320
Asp	Pro	Val	Thr	Ile 325	Glu	Asn	Lys	Gly	Ser 330	Thr	Pro	Gln	Thr	Tyr 335	Lys
Val	Ile	Ser	Thr 340	Leu	Thr	Ile	Ser	Glu 345	Ile	Asp	Trp	Leu	Asn 350	Leu	Asn
Val	Tyr	Thr 355	Cys	Arg	Val	Asp	His 360	Arg	Gly	Leu	Thr	Phe 365	Leu	Lys	Asn
Val	Ser 370	Ser	Thr	Суѕ	Ala	Ala 375	Ser	Pro	Ser	Thr	Asp 380	Ile	Leu	Asn	Phe
Thr 385	Ile	Pro	Pro	Ser	Phe 390	Ala	Asp	Ile	Phe	Leu 395	Ser	Lys	Ser	Ala	Asn 400
Leu	Thr	Cys	Leu	Val 405	Ser	Asn	Leu	Ala	Thr 410	Tyr	Glu	Thr	Leu	Ser 415	Ile
Ser	Trp	Ala	Ser 420	Gln	Ser	Gly	Glu	Pro 425	Leu	Glu	Thr	Lys	Ile 430	Lys	Ile
Met	Glu	Ser 435	His	Pro	Asn	Gly	Thr 440	Phe	Ser	Ala	Lys	Gly 445	Val	Ala	Ser
Val	Cys 450	Val	Glu	Asp	Trp	Asn 455	Asn	Arg	Lys	Glu	Phe 460	Val	Суз	Thr	Val
Thr 465	His	Arg	Asp	Leu	Pro 470	Ser	Pro	Gln	Lys	Lys 475	Phe	Ile	Ser	Lys	Pro 480
Asn	Glu	Val	His	Lys 485	His	Pro	Pro	Ala	Val 490	Tyr	Leu	Leu	Pro	Pro 495	Ala
Arg	Glu	Gln	Leu 500	Asn	Leu	Arg	Glu	Ser 505	Ala	Thr	Val	Thr	Cys 510	Leu	Val
Lys	Gly	Phe	Ser	Pro	Ala	Asp	Ile	Ser	Val	Gln	Trp	Lys	Gln	Arg	Gly

JUL 2 1 2000 JUL 2

515

520

525

Gln Leu Leu Pro Gln Glu Lys Tyr Val Thr Ser Ala Pro Met Pro Glu 530 535 540

Pro Gly Ala Pro Gly Phe Tyr Phe Thr His Ser Ile Leu Thr Val Thr 545 550 555 560

Glu Glu Glu Trp Asn Ser Gly Glu Thr Tyr Thr Cys Val Val Gly His 565 570 575

Glu Ala Leu Pro His Leu Val Thr Glu Arg Thr Val Asp Lys Ser Thr
580 585 590

Gly Lys Pro Thr Leu Tyr Asn Val Ser Leu Ile Met Ser Asp Thr Gly 595 600 605

Gly Thr Cys Tyr 610

Enelwing Gly